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RACIAL DIFFERENCES IN BLADDER CANCER RISK: A CASE-CONTROL STUDY

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To determine why the incidence rate of transitional cell bladder cancer in whites in the United States is approximately twice that in blacks, the authors examined data from a large population-based case-control study of bladder cancer conducted in 1978 involving 2,982 cases and 5,782 controls. The relative risk of transitional cell carcinoma for whites compared with blacks was 1.9 before adjustment for the major bladder cancer risk factors, whereas after adjustment for cigarette smoking and occupation it was 1.6 (95% confidence interval (CI): 1.3–2.1). Further adjustment for other risk factors, including history of a bladder infection and a family history of urinary tract cancer, did not alter this estimate. The elevated risk of whites compared with blacks was limited, however, to cases whose disease was confined to the mucosa and submucosa. Among cases whose disease had extended to the bladder musculature or beyond, whites were at slightly reduced risk compared with blacks. This suggests that whites may be diagnosed with conditions that go undetected in blacks but that are unlikely as a group to progress to more extensive disease. Because of the population-based nature of the study, it was possible to determine that if bladder cancer incidence among whites of both sexes was reduced to the level among blacks, total incidence in the United States would fall by 36 per cent.

adenocarcinoma; blacks; bladder neoplasms; carcinoma, squamous cell; carcinoma, transitional cell; whites

The incidence rate of bladder cancer in the United States among white males is approximately twice that among black males, while that among white females is approximately 40–50 per cent higher than that among black females (1). Blacks have poorer five-year survival rates than do whites, however, largely because they tend to be diagnosed at later stages of disease (2–4). The increased incidence of bladder tumors in whites may be due, in part, to different risk factors operating in the black and the white populations. Whites may also have had more exposure to known bladder cancer risk factors, particularly high-risk occupations (2, 5) and cigarette smoking. Additionally, innate differences in the ability to deactivate certain environmental carcinogens may play a role in modifying susceptibility to bladder cancer (6). The greater disparity between incidence rates than between mortality rates also suggests the possibility that differential use of di-

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agnostic services could account for part of the difference in incidence rates (7).

To explore further the reasons for the higher incidence rate in whites than in blacks, we examined interview data from a large population-based case-control study of bladder cancer.

Materials and methods

Cases consisted of residents of metropolitan Atlanta, Georgia; Detroit, Michigan; New Orleans, Louisiana; San Francisco, California; Seattle, Washington; and the states of Connecticut, Iowa, New Mexico, Utah, and New Jersey, aged 21–84 years, who were identified through the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (8) or the New Jersey Cancer Registry during a one-year period beginning in December 1977 as having newly diagnosed, histologically proven cancer of the urinary bladder.

Controls consisted of an age- and sex-stratified random sample of the general population in the 10 geographic areas; an approximately 2:1 frequency-matching ratio of controls to cases was used. Controls aged 21–64 years were chosen through random-digit dialing. Controls aged 65–84 years were randomly selected from rosters maintained by the Health Care Financing Administration, Baltimore, MD. Details of the study methods have been presented elsewhere (9).

A total of 4,086 eligible cases were identified during the study period, and most were contacted for interview within 90 days of diagnosis. Of the 3,763 cases alive at the time of contact, 2,982 (73 per cent of eligible cases) were interviewed. A total of 5,782 (83 per cent) of 6,985 eligible controls were interviewed. Although we do not have response rates available by race, our results are in general agreement with SEER incidence rates, suggesting that response rates did not differ substantially for blacks and for whites.

Information on the histologic type of bladder cancer was available from hospital records for 2,915 (98 per cent) interviewed cases: 2,834 had transitional cell carcinoma, 43 had squamous cell carcinoma, 32 had adenocarcinoma, and six had undifferentiated or anaplastic carcinoma. For cases identified in those areas covered by the SEER Program, information regarding the stage of the tumor at diagnosis was also available from the SEER Program. Because New Jersey was not a SEER participant in 1978, information on stage at diagnosis was not available for the 27 per cent of black cases and 32 per cent of white cases in the study who were diagnosed in New Jersey. Among those for whom SEER records were presumably available, a substantially higher percentage of blacks than whites (22 vs. 9 per cent) had missing information on stage at diagnosis.

To supplement results from the case-control study, we examined incidence data from the SEER Program for the years 1973–1983. For cases diagnosed between 1977 and 1982 in nine SEER areas (i.e., San Francisco-Oakland, California; Connecticut; Detroit, Michigan; Hawaii; Iowa; New Mexico; Seattle, Washington; Utah; and Atlanta, Georgia), stage at diagnosis was also available (10).

Personal interviews were conducted in the homes of respondents by trained interviewers. Information was elicited on demographic characteristics, lifetime tobacco use, family history of urinary tract cancer, history of bladder infections, coffee consumption, use of artificial sweeteners, history of bladder and kidney stones, and occupation. For purposes of analysis, occupations that involved exposure to dye, rubber, leather, ink, or paint were considered a priori to entail higher bladder cancer risk since these substances have been linked to risk of bladder cancer (11). In addition, occupations with elevated smoking-adjusted relative risks and a total of at least 15 cases and controls were identified for white males, nonwhite males, white females, and nonwhite females separately

(23). Elevated relative risks were defined in two ways, as equal to or greater than 1.1 and as equal to or greater than 1.5. Because controlling for occupations defined as having a relative risk of 1.1 or more minimized the relative risk of whites compared with blacks, we have chosen to present results using this definition. Approximately 45 such occupations were identified for white males, 23 for nonwhite males, 16 for white females, and six for nonwhite females.

To measure the effect of exposure on disease, we estimated relative risks and 95 per cent confidence intervals using polychotomous logistic (12) and binary logistic regression (13) models. Binary logistic regression was also used to evaluate the statistical significance of interactions. Population attributable risks were calculated using the method of Bruzzi et al. (14).

RESULTS

Relative risks of bladder cancer associated with race according to histologic type are shown in table 1. Among cases with transitional cell carcinoma, whites had a relative risk of 1.9 (95 per cent confidence interval (CI): 1.5–2.3) compared with blacks. Among males, the relative risk was 1.8 (95 per cent CI: 1.4–2.4) for whites compared with blacks, while among females, it was 2.1 (95 per cent CI: 1.3–3.3). Among cases with squamous cell carcinoma or adenocarcinoma, on the other hand, whites were at lower risk than were blacks (relative risk (RR) = 0.6, 95 per cent CI: 0.2–1.4, and RR = 0.3, 95 per cent CI: 0.1–0.6, respectively).

These results generally agree with SEER average annual age-adjusted incidence rates for 1973–1983, as shown in table 2. The incidence (per 100,000 population) of transitional cell carcinoma among whites was twice that among blacks (14.71 vs. 7.38). Among males, whites had more than twice the rate of blacks (26.19 vs. 11.84), while among females the incidence rate for whites was 1.6 times that for blacks (6.39 vs. 4.09). As in our data, the incidence rates of squamous cell carcinoma and adenocarcinoma among whites were lower than those among blacks.

As shown in figure 1, the incidence rates of transitional cell bladder cancer in white males were higher than those in black males at all ages, based on data collected by the SEER Program during 1973–1983. Similarly, white females had consistently higher rates than did black females, particularly at ages less than 55 years.

Table 3 shows the relative risk of transitional cell bladder cancer associated with several suspected risk factors by race. Cigarette smoking significantly increased risk by more than twofold in both blacks and whites. When we examined more specific smoking parameters, ex-smokers had relative risks intermediate between nonsmokers and current smokers, risk increased with dose and duration of smoking,

TABLE 1

*Relative risk (RR) associated with race according to histologic type of bladder cancer, United States, 1978**

	Blacks		Whites		RR†	95% CI‡
	n	%	*n*	%		
Controls	403		5,258			
Cases						
Total	122		2,739			
Transitional cell	110	90	2,679	98	1.9	1.5–2.3
Squamous cell	5	4	36	1	0.6	0.2–1.4
Adenocarcinoma	7	6	24	1	0.3	0.1–0.6

* Excluding other races and other and unknown histologies.

† Relative risk of whites compared with blacks, adjusted for sex and age.

‡ CI, confidence interval.

TABLE 2

*Average annual age-adjusted (1970 standard) incidence rates (per 100,000 population) for carcinomas of the urinary bladder in the United States, by sex, race, and histologic type, 1973–1983**

	Transitional cell		Squamous cell		Adenocarcinoma	
	No. of cases	Rate	No. of cases	Rate	No. of cases	Rate
Both sexes						
Black	1,122	7.38	106	0.71	61	0.37
White	30,076	14.71	702	0.34	427	0.21
Males						
Black	770	11.84	55	0.89	33	0.46
White	22,504	26.19	392	0.46	281	0.33
Females						
Black	352	4.09	51	0.60	28	0.31
White	7,572	6.39	310	0.25	146	0.13

* From the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute (8).

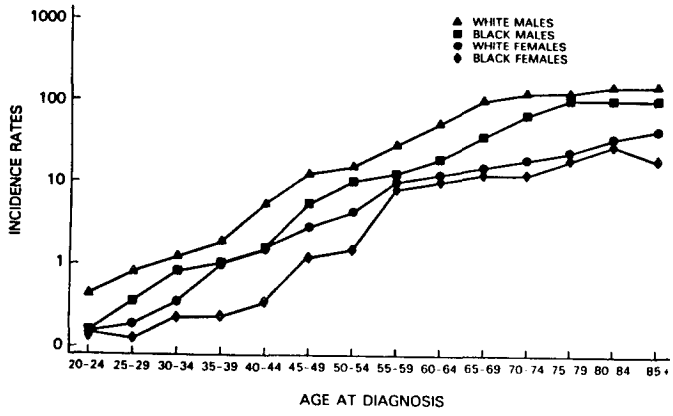

FIGURE 1. Age-specific incidence rates of transitional cell bladder cancer for white males, black males, white females, and black females, United States, 1973–1983.

and those who had smoked only filter cigarettes had risks intermediate between nonsmokers and those who had ever smoked nonfilter cigarettes in both races. Exposure to dye, rubber, leather, ink, or paint did not increase risk among blacks (RR = 0.8, 95 per cent CI: 0.5–1.4), but was associated with a slight increase among whites (RR = 1.3, 95 per cent CI: 1.2–1.4). The relative risk associated with employment in occupations determined a posteriori to increase risk was 1.7 in blacks (95 per cent CI: 1.0–2.7) and 1.4 in whites (95 per cent CI: 1.2–1.6), but these occupations were not necessarily the same in both races. A history of a bladder infection significantly increased risk in both blacks (RR = 2.1, 95 per cent CI: 1.2–3.8) and whites (RR = 1.6, 95 per cent CI: 1.4–1.8). Although risk associated with a family history of urinary tract cancer was also elevated among both blacks (RR = 1.3, 95 per cent CI: 0.3–6.8) and whites (RR = 1.4, 95 per cent CI: 1.1–1.7), the estimate among blacks was based on few exposed persons. None of the differences in relative risk between blacks and whites was statistically significant.

To determine whether the higher incidence of transitional cell bladder cancer in whites could be due to greater exposure to these risk factors than in blacks, we examined the proportion of exposed among both black and white controls (table 4). A total of 57 per cent of whites compared with 54 per cent of blacks had ever smoked

TABLE 3

*Relative risks (RR) associated with suspected risk factors for transitional cell bladder cancer by race, United States, 1978**

Risk factor	Blacks				Whites			
	No. of cases	No. of controls	RR†	95% CI‡	No. of cases	No. of controls	RR†	95% CI
Ever smoked								
No	21	159	1.0		543	1,851	1.0	
Yes	79	227	2.7	1.5–4.6	1,997	3,174	2.2	2.0–2.5
Exposure to dye, rubber, leather, ink, or paint								
No	75	284	1.0		1,637	3,571	1.0	
Yes	25	102	0.8	0.5–1.4	903	1,454	1.3	1.2–1.4
Worked in occupation with relative risk of 1.1 or more								
No	32	171	1.0		444	1,210	1.0	
Yes	68	215	1.7	1.0–2.7	2,096	3,815	1.4	1.2–1.6
History of a bladder infection								
No	76	339	1.0		2,037	4,338	1.0	
Yes	24	47	2.1	1.2–3.8	503	687	1.6	1.4–1.8
Family history of urinary tract cancer								
No	98	379	1.0		2,399	4,817	1.0	
Yes	2	7	1.3	0.3–6.8	141	208	1.4	1.1–1.7

* Excluding subjects with missing values.

† Each relative risk adjusted for other risk factors, sex, and age.

‡ CI, confidence interval.

cigarettes. A somewhat higher percentage of blacks than whites were current smokers (29 vs. 24 per cent), while whites were more frequently ex-smokers (33 vs. 25 per cent). Blacks and whites differed little according to duration of smoking. A higher percentage of whites than blacks, however, had ever smoked nonfilter cigarettes (56 vs. 50 per cent) or had smoked 20 or more cigarettes per day (38 vs. 24 per cent). A slightly higher percentage of whites than blacks had ever been exposed to dye, rubber, leather, ink, or paint (29 vs. 27 per cent), whereas a considerably higher percentage of whites were employed in occupations determined a posteriori to increase risk of bladder cancer (75 vs. 55 per cent). Slightly higher percentages of whites than blacks reported a history of a bladder infection (14 vs. 12 per cent) or a family history of urinary tract cancer (4 vs. 2 per cent).

Relative risks associated with race among cases with transitional cell bladder cancer after adjustment for cigarette smoking and occupational variables are shown in table 5. Ever having smoked cigarettes only slightly confounded the association with race, reducing the relative risk from 1.9 to 1.8. Adjustment for more specific measures of smoking, including current and past smoking (smoking status), duration of smoking, and filtration yielded similar results. Control for dose of smoking, on the other hand, reduced the relative risk to 1.7 due to the higher percentage of whites who had smoked heavily. Because a higher percentage of blacks than whites were current smokers, however, the relative risk of whites compared with blacks was 1.8 when adjusted for dose according to past and current smoking. Similarly, control for occupational exposure to substances suspected a priori of increasing risk of bladder cancer only slightly reduced the relative risk to 1.8, while control for a posteriori high-risk occupations resulted in a relative risk of 1.7 due to the larger percentage of whites compared with blacks who were employed in such occupations. Simultaneous adjustment for dose according to past and

TABLE 4

Percentages of black and of white controls according to bladder cancer risk factors, United States, 1978*

Risk factor	Blacks (%)	Whites (%)
Smoking status		
Nonsmoker	42	38
Ex-smoker	25	33
Current smoker	29	24
Years smoked		
Nonsmoker	42	38
1–19	11	12
20–39	23	23
40–59	18	20
≥60	2	2
Filtration		
Nonsmoker	42	38
Filter only	8	6
Filter and nonfilter	27	30
Nonfilter only	23	26
Usual no. of cigarettes/day		
Nonsmoker	42	38
1–19	30	19
20–39	20	28
≥40	4	10
Ever exposed to dye, rubber, leather, ink, or paint (a priori)		
No	74	72
Yes	27	29
Employment in high-risk occupation (a posteriori)†		
No	44	24
Yes	55	75
Bladder infection		
No	88	86
Yes	12	14
Family history of urinary tract cancer		
No	97	96
Yes	2	4

* Percentages are age-adjusted.

† Occupations with a relative risk of 1.1 or more.

current smoking and for a priori and a posteriori high-risk occupations yielded a relative risk of 1.6 (95 per cent CI: 1.3–2.1). Further adjustment for a history of bladder infections, a family history of urinary tract cancer, and education did not alter this estimate.

After adjustment for dose according to past and current smoking and a priori and a posteriori high-risk occupations, white females remained at twice the risk of black females (95 per cent CI: 1.3–3.3), whereas white males were at 50 per cent increased risk compared with black males (95 per cent CI: 1.2–2.0). When subjects were limited to those who were unexposed to the major bladder cancer risk factors, i.e., nonsmokers without a family history of urinary tract cancer or history of a bladder infection who had never been employed in an a posteriori high-risk occupation, whites were at even higher risk compared with blacks (RR = 3.2, 95 per cent CI: 1.1–9.1). Among unexposed females, who comprised 60 per cent of those unexposed, there was only one black case, yielding an unstable estimate of the relative risk for whites compared with blacks. Among unexposed males, the relative risk for whites compared with blacks was 1.9 (95 per cent CI: 0.6–6.6).

As shown in table 6, after adjustment for smoking and occupation, risk of transitional cell carcinoma associated with being white varied considerably according to stage at diagnosis, falling steadily from 5.0 when malignancy was in situ or confined to the mucosa to 0.7 when malignancy had extended beyond the bladder. In view of the small number of blacks for whom data on the stage of cancer were available in our study, we also examined rates according to stage at diagnosis using SEER data for the years 1977–1982. Among cases with in situ disease or disease confined to the mucosa, the incidence rate for whites was nearly 3.5 times that for blacks. As the degree of invasion increased from the submucosa to the superficial muscle to the deep musculature, incidence rates for whites were 2.5, 1.7, and 1.5 times those for blacks, respectively. Among cases whose disease had extended into the surrounding connective tissue, however, whites and blacks had approximately the same incidence rates. Approximately 5 per cent of the records for both blacks and whites were unstaged.

Table 7 presents estimates of risk attributable to the major risk factors for bladder cancer according to race. Among both blacks and whites, smoking accounted for the highest portion of risk (48 and 43 per

TABLE 5

Relative risk associated with race among cases with transitional cell bladder cancer after adjustment for cigarette smoking and occupational variables, United States, 1978

Adjustment*	Blacks	Whites	95% CI†
Age and sex only	1.0	1.9	1.5–2.3
Ever smoked	1.0	1.8	1.4–2.3
Smoking status‡	1.0	1.9	1.5–2.4
Duration of smoking	1.0	1.9	1.5–2.3
Filtration	1.0	1.8	1.4–2.3
Dose of smoking	1.0	1.7	1.4–2.2
Status‡ and dose of smoking	1.0	1.8	1.4–2.2
A priori high-risk occupations	1.0	1.8	1.5–2.3
A posteriori high-risk occupations	1.0	1.7	1.4–2.2
Dose according to smoking status,‡ and a posteriori and a priori high-risk occupations	1.0	1.6	1.3–2.1

* All relative risks adjusted for age and sex.

† CI, confidence interval.

‡ Smoking status: nonsmoker, ex-smoker, or current smoker.

TABLE 6

Relative risk (RR) of transitional cell bladder cancer associated with race according to stage at diagnosis, United States, 1978†*

	Blacks		Whites		Unadjusted RR‡	Adjusted RR§	95% CI‖
	n	%	*n*	%			
Controls	290		3,716				
Cases							
Total	38		1,021				
In situ or mucosa	7	18	468	46	5.3	5.0	2.3–10.7
Submucosa	8	21	275	27	2.7	2.4	1.2–4.9
Extended to bladder musculature	14	37	192	19	1.1	0.9	0.5–1.6
Beyond bladder	9	24	86	8	0.7	0.7	0.3–1.4

* Relative risk for whites compared with blacks.

† Excluding other races, unstaged cases, and subjects residing in New Jersey.

‡Adjusted for sex and age.

§ Adjusted for sex, age, dose according to whether ex- or current smoker, and a priori and a posteriori high-risk occupations.

‖ CI, confidence interval.

TABLE 7

Attributable risk associated with bladder cancer risk factors among blacks and whites, United States, 1978

Risk factor	Blacks			Whites		
	Estimated RR*	% cases exposed	Attributable risk (%)	Estimated RR*	% cases exposed	Attributable risk (%)
Smoking	2.6	78	48	2.2	78	43
Occupation†	1.5	65	22	1.5	85	28
Bladder infection	2.3	26	15	1.7	20	8
Family history of urinary tract cancer	1.4	3	1	1.4	6	2
Total			66			63

* Relative risks (RR) adjusted for other risk factors, age, and sex.

† Among whites ever exposed to dye, rubber, leather, ink, or paint, *or* employed in an occupation with a relative risk of 1.1 or more and among blacks employed in an occupation with a relative risk of 1.1 or more (23).

cent, respectively). Exposure to occupations with a relative risk of 1.1 or more accounted for 22 per cent of bladder cancer in blacks, while exposure to dye, rubber, leather, ink, or paint or occupations with a relative risk of 1.1 or more accounted for 28 per cent of bladder cancer in whites. History of a bladder infection contributed to approximately twice as much disease in blacks as in whites (15 vs. 8 per cent). Due to its rarity, a family history of urinary tract cancer contributed little to risk of disease in either race. Overall, approximately 66 per cent of bladder cancer in blacks and 63 per cent in whites was attributable to these factors. When we examined attributable risk specific for sex, we found that the major risk factors accounted for 70 per cent of bladder cancer in white males, 48 per cent in white females, 60 per cent in black males, and 74 per cent in black females. In addition, we calculated that if bladder cancer incidence among whites of both sexes was reduced to the level among blacks, the total incidence in the United States would fall by 36 per cent.

Discussion

In the United States, the incidence rate of transitional cell carcinoma of the bladder, which comprises approximately 90 per cent of bladder tumors, is approximately twice as high in whites as in blacks, while squamous cell carcinomas and adenocarcinomas are about half as common in whites compared with blacks. Mortality rates for blacks and whites, on the other hand, show less disparity than do incidence rates. Although mortality rates among white males remained fairly constant between 1935 and 1973–1974, while mortality rates for nonwhite males increased during the same period, whites nevertheless had 25 per cent higher mortality rates than did nonwhites in 1973–1974 (15). In contrast, during the same period, mortality rates for white females decreased while those for nonwhite females increased slightly, leaving nonwhite females with a 50 per cent excess mortality compared with whites in 1973 (15). SEER mortality data indicate that white males had a 40 per cent higher mortality than did black males between 1973 and 1983, whereas black females continued to have a 50 per cent excess mortality compared with white females (8).

SEER incidence data indicate that sex and age are major risk factors for bladder cancer among both blacks and whites. Our data show that cigarette smoking, history of a bladder infection, and a family history of urinary tract cancer also increased risk in both races. Occupational exposures to dye, rubber, leather, ink, or paint slightly increased risk in whites but not in blacks. Although occupations determined a posteriori to increase risk were not necessarily the same in blacks and whites, the relative risks associated with these occupations were similar in both races. Approximately 66 per cent of bladder cancer in blacks and 63 percent in whites were attributable to these factors, suggesting that there are some unidentified risk factors for bladder cancer.

It has been suggested that differential exposure to certain of these risk factors among blacks and whites could account, in part, for the higher incidence rate in whites. Wynder and Kabat (5) hypothesized that more frequent employment of whites in industries that have been shown to increase risk of bladder cancer may partially explain the higher rates in whites. However, the percentage of whites exposed to dye, rubber, leather, ink, or paint, substances that have been shown to increase risk of bladder cancer (11), was approximately the same as that of blacks in our data. Thus, control for this variable did not substantially alter the risk of whites compared with blacks. A higher percentage of whites than blacks were, however, employed in occupations determined a posteriori to increase risk of bladder cancer. Adjustment for this variable therefore reduced the relative risk of bladder cancer in whites compared with blacks. We note, however, that because of

the small number of blacks in our study compared with whites, certain occupations with a relative risk of 1.1 or more may have been identified in whites but not in blacks because there were fewer than 15 black cases and controls employed in the occupation. Although defining high-risk occupations as those with a relative risk of 1.1 or more also undoubtedly included chance findings in the high-risk group, we chose to use this definition because it minimized the relative risk of whites compared with blacks.

Because cigarette smoking is a well-established risk factor for bladder cancer (11, 16), it is possible that differences in smoking habits between blacks and whites could explain a substantial portion of the difference in incidence rates. This was not the case, however. Although white controls were more likely to have ever smoked, smoked more heavily, and used nonfilter cigarettes more frequently than were black controls, a higher percentage of blacks were current smokers. Approximately equal percentages of blacks and whites were smokers of long duration. Therefore, adjustment for the effects of cigarette smoking only slightly reduced the risk of transitional cell bladder cancer for whites compared with blacks. The patterns of smoking in our data generally reflect those from the National Health Interview Surveys conducted between 1978 and 1980. Data combined over the three years indicate that while whites were more frequently heavy smokers, blacks had a higher prevalence of smoking (17). The 1979 survey also indicates that among current smokers, blacks tended to smoke products with a higher concentration of tar than those used by whites, but the lower number of cigarettes they smoked daily probably resulted in a lower average daily dose of smoke constituents (18).

Adjustment for other bladder cancer risk factors, including a family history of urinary tract cancer, a history of a bladder infection, and sociodemographic variables such as education, also did not appreciably alter risk estimates associated with race. It is possible, however, that blacks and whites experienced different degrees of exposure to environmental factors that were unaccounted for in our analysis.

It is also possible that innate racial differences in the ability to activate or deactivate environmental carcinogens could contribute to the difference in rates between blacks and whites. In particular, humans have been shown to differ in their capacities to detoxify arylamines (chemical carcinogens used in certain occupational settings) by *N*-acetylation, suggesting that persons with slow acetylator phenotypes may have greater susceptibility to arylamine-induced bladder cancer than those with fast acetylator phenotypes (19). There is some epidemiologic evidence to support this suggestion (19), but we are unaware of any studies to date that have examined whether differences in acetylator phenotype are related to race. Although our ability to assess occupational exposure to arylamines was limited, our data do not suggest strong racial differences in susceptibility to occupationally induced bladder cancer. We also found little evidence of racial differences in the ability to process carcinogens found in cigarette smoke.

The smaller disparity between mortality rates than between incidence rates for blacks and whites suggests that the difference in incidence rates may be due in part to differential use of diagnostic services (7). It is well documented that survival rates for blacks are poorer than those for whites (2–4), largely because disease in whites is more frequently diagnosed in the localized stage (78 vs. 61 per cent for white males vs. black males; 72 vs. 56 per cent for white females vs. black females) (3). Our data are in agreement with previous reports (2), which show that whites tend to be diagnosed at earlier stages than do blacks. In fact, the elevated risk of whites with transitional cell carcinoma compared with blacks was confined to cases diagnosed with in situ disease or disease limited to the

mucosa or submucosa. Among cases diagnosed with disease which had extended to the musculature or beyond, whites were not at elevated risk compared with blacks. Adjustment for the major bladder cancer risk factors did not substantially alter these results. Data from the SEER Program for 1977–1982 also show the highest rates for whites compared with blacks among cases with in situ disease or disease confined to the mucosa.

A survey among blacks, commissioned by the American Cancer Society, showed that urban blacks, particularly those with low household incomes, tend to be less knowledgeable than the general population about early warning signals for cancer and less likely to see a doctor if they experience symptoms (unpublished data). This differential use of diagnostic services coupled with a number of difficulties in the diagnosis of superficial bladder tumors may partially account for the higher rates of transitional cell bladder cancer in whites than in blacks. In particular, there has been considerable controversy over whether papillary growths of the urothelium behave in a "benign" or "malignant" manner (20). For many years, these lesions were classified as low-grade carcinoma, whereas recent evidence suggests that many of them may follow a relatively benign course (20, 21). It is possible, therefore, that whites, because of their heightened awareness of cancer warning signals and increased use of diagnostic services, are diagnosed with conditions that go undetected in blacks but that on average are less likely to progress to advanced disease. Although it is possible that the use of health services is positively associated with social class in both races, adjustment for education, the only socioeconomic variable available, did not affect the difference in risk between blacks and whites. This may mean that at similar levels of education, whites are still more likely to see a doctor than are blacks and consequently are more likely to be diagnosed with conditions which follow a relatively benign course.

Alternatively, it is possible that painless hematuria, the presenting symptom of 68–97 per cent of bladder cancers (22), is unlikely to be ignored by either race. This would suggest that blacks for some reason do not develop noninvasive disease as frequently as do whites.

In summary, it appears that the higher incidence rates of transitional cell bladder cancer in whites may be due, in part, to more frequent diagnosis of early papillary lesions. The fact that mortality rates for white males remain higher than those for black males suggests, however, that diagnostic differences do not totally account for the difference in incidence rates, at least in males. Other factors that appear to contribute to the observed excess in whites include confounding due to the effects of smoking and certain occupational carcinogens. It is also possible that differences in risk factors as yet undetected could contribute to the difference in rates, but these would have to be risk factors for the less invasive tumors rather than for the whole spectrum of disease.

References

1. Cutler SJ, Young JL Jr., eds. Third National Cancer Survey: incidence data. Natl Cancer Inst Monogr 1975;41:23.
2. Seidman H, Silverberg E, Holleb AI. Cancer statistics, 1976: A comparison of white and black populations. Cancer J Clin 1976;26:2–29.
3. Myers MH. Survival from cancer by blacks and whites. In: Mettlin C, Murphy GP, eds. Cancer among black populations. New York: Alan R. Liss, Inc., 1981:151–65.
4. Young JL, Ries LG, Pollack ES. Cancer patient survival among ethnic groups in the United States. JNCI 1984;73:341–52.
5. Wynder EL, Kabat GC. Opportunities for prevention of cancer in blacks. In: Mettlin C, Murphy GP, eds. Cancer among black populations. New York: Alan R. Liss, Inc., 1981:237–52.
6. Calabrese EJ. Is the role of the environment in carcinogenesis overestimated? Med Hypoth 1979; 5:5–14.
7. Morrison AS, Cole P. Epidemiology of bladder cancer. Urol Clin North Am 1976;3:13–29.
8. Young JL Jr, Percy CL, Asire AJ. Surveillance, epidemiology, and end results: incidence and mortality data: 1973–1977. Natl Cancer Inst Monogr 1981;57:1–1082.
9. Hartge P, Cahill JI, West D, et al. Design and methods in a multi-center case-control interview study. Am J Public Health 1984;74:52–6.

10. American joint committee on cancer. Manual for staging of cancer. 2nd ed. Beahrs OH, Myers MH, eds. Philadelphia, PA: J. B. Lippincott Co., 1983.
11. Matanoski GM, Elliott EA. Bladder cancer epidemiology. Epidemiol Rev 1981;3:203–29.
12. Dubin N, Pasternack BS. Risk assessment for case-control subgroups by polychotomous logistic regression. Am J Epidemiol 1986;123:1101–17.
13. Breslow NE, Day NE. Statistical methods in cancer research. Vol. 1. The analysis of case-control studies. Lyon: IARC, 1980:192–244.
14. Bruzzi P, Green SB, Byar DP, et al. Estimating the population attributable risk for multiple risk factors using case-control data. Am J Epidemiol 1984;122:904–14.
15. Devesa SS, Silverman DT. Cancer incidence and mortality trends in the United States: 1935–74. JNCI 1978;60:545–71.
16. Hartge P, Silverman D, Hoover R, et al. Changing cigarette habits and bladder cancer risk: a case-control study. JNCI 1987;78:1119–25.
17. US Department of Health and Human Services. The health consequences of smoking: cancer and chronic lung disease in the workplace. A report of the Surgeon General. Washington, DC: US GPO, 1985. (DHHS (PHS) 85-50207).
18. US Department of Health and Human Services. The health consequences of smoking: the changing cigarette. A report of the Surgeon General. Washington DC: US GPO, 1981. (DHHS (PHS) 81-50156).
19. Lower GM. Arylamines and bladder cancer causality: application of conceptual and operational criteria. Clin Pharmacol Ther 1983;34:129–35.
20. Brawn PN. Interpretation of bladder biopsies. New York: Raven Press, 1984.
21. Zingg EJ, Wallace DMA. The treatment of superficial bladder tumors. In: Zingg EJ, Wallace DMA, eds. Bladder cancer. New York: Springer-Verlag, 1985:161–87.
22. Zingg EJ, Wallace DMA. Symptomatology. In: Zingg EJ, Wallace DMA, eds. Bladder cancer. New York: Springer-Verlag, 1985:77–85.
23. Silverman DT, Hoover RN, Levin L. Occupation and bladder cancer in the United States. (unpublished manuscript).